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Early melanoma detection and acral lentiginous melanoma: evidence from Central-Eastern Europe

Summary of the Ph.D. thesis

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LIST OF PUBLICATIONS

This doctoral thesis is based on the following publications (total impact factor: 6.515):

- I Csányi, N Houshmand, M Szűcs, H Ócsai, L Kemény, J Oláh, E Baltás. Acral lentiginous melanoma: a single-center retrospective review of four decades in East-Central Europe. J Eur Acad Dermatol Venereol. 2020;34(9):2004-2010. **D1, IF: 6.166**
- I Petrovszki, I Csányi, M Szűcs, H Ócsai, N Houshmand, L Kemény, J Oláh, E Baltás. Factors influencing early detection of malignant melanoma. Orvosi Hetilap. 2016;157(51):2028-2033. **Q4, IF: 0.349**

Publications not directly related to the thesis (total imapct factor: 17.4*):

- NK Kovács, ÁÁ Balogh, I Csányi, M Manczinger, AT Fülöp, L Asztalos, J Dombi, G Weszelovszky, R Gyulai, L Kemény, E Baltás. Image-based education enhances public accuracy in identifying concerning pigmented skin lesions. [*submitted for publication*]
- BT Papp, K Toplenszky, H Ócsai, I Csányi, L Kemény, R Gyulai, J Oláh, E Baltás. Ten Years of Euromelanoma in Hungary: Nationwide Trends and Risk Factors for Skin Cancer in Central–Eastern Europe. Cancers. 2025;17(23):3749. **Q1, IF: 4.4***
- B Nagy, N Kovács, K Ónodi, I Csányi, H Ócsai, J Oláh, L Kemény, R Gyulai, E Baltás. Skin-directed therapies in early-stage mycosis fungoides. Bőrgyógyász Venerol Szle. 2025;101(5):261-267.
- P Rózsa, BT Papp, E Szederkény, G Vass, Cs Hánis, I Csányi, H Ócsai, E Baltás, J Oláh, L Kemény, R Gyulai, E Kis. Electrochemotherapy for multiple nonmelanoma skin tumors in immunosuppressed patients: a prospective cohort analysis. J Dermatol Ther. 2025. **Q1, IF: 3.4***
- P Rózsa, I Csányi, G Vass, E Varga, IB Németh, I Korom, H Ócsai, E Baltás, J Oláh, R Gyulai, E Kis. Electrochemotherapy, as a novel therapeutic approcach in the management of lentigo maligna, lentigo maligna melanoma and acral lentiginous melanoma. J Dermatol Treat. 2025;36(1):2495096. **Q1, IF: 3.9***
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1. INTRODUCTION

1.1. Acral melanoma

1.1.1. Terminology, classification and pathogenesis

Acral melanoma (AM) refers to melanomas arising on glabrous (non-hair-bearing) skin of the extremities (palms, soles, heels, fingers) and nail apparatus, irrespective of histological subtype. In contrast, acral lentiginous melanoma (ALM), first described by Reed in 1976, denotes a distinct histopathological growth pattern characterized by lentiginous proliferation of atypical melanocytes along the dermoepidermal junction, accompanied by epidermal hyperplasia and dermal inflammation. While ALM represents the most common histological subtype at acral sites, not all acral melanomas exhibit a lentiginous growth pattern.

Multiple melanoma subtypes may occur on acral skin, including superficial spreading melanoma (SSM), nodular melanoma (NM), and desmoplastic melanoma (DM). Reported proportions of ALM vary widely (40–80%), largely due to differences in anatomical definitions and classification criteria. Histological subtype distribution is strongly site-dependent: palmoplantar and subungual melanomas predominantly show a lentiginous pattern, whereas dorsal aspects of the hands and feet more frequently harbour SSM and NM.

According to the 2018 WHO classification, acral melanoma belongs to the group of melanomas not consistently associated with ultraviolet (UV) radiation. It is characterized by a low UV mutational signature, relatively low tumor mutational burden, and frequent copy-number alterations and structural chromosomal rearrangements. Activating BRAF and NRAS mutations occur less frequently than in UV-driven cutaneous melanoma, while KIT alterations and complex genomic changes are more common. These molecular features distinguish acral melanoma biologically and therapeutically from other cutaneous melanoma subtypes.

The pathogenesis of AM differs fundamentally from UV-induced melanoma. Acral skin, has distinct anatomical characteristics, including a thick stratum corneum and the absence of hair follicles. Non-UV-related mechanisms, site-specific microenvironmental factors, and intrinsic biological differences of acral melanocytes—including positional gene expression programs—are thought to contribute to tumor initiation and progression. Mechanical stress and repeated trauma at weight-bearing and high-pressure sites, such as the soles and palms, have been proposed as contributory factors in tumor initiation and progression, but evidence on their role is not clear so far.

1.1.2. Epidemiology and diagnosis

Although the global incidence of melanoma continue to rise in light-skinned populations, AM remains rare in Caucasians, accounting for less than 10% of cases in Europe and in the United States. In contrast, AM represents a substantially larger portion of melanomas in Asian (30-46%) and African (50-70%) populations. In Hungary and other Central-European countries, SSM is the predominant subtype, whereas AM is among the least frequently diagnosed forms. Clinical recognition of AM is challenging due to its concealed localisation, variable appearance, and relatively high proportion of amelanotic lesions. Dermoscopy plays a key role in early diagnosis, particularly the parallel-ridge pattern on volar skin, which has high sensitivity and specificity for AM. Diagnostic algorithms such as the BRAAFF checklist further improve accuracy. In nail unit melanoma, irregular longitudinal pigmentation and periungual extension (Hutchinson's sign) are critical warning signs. Despite these clues, diagnostic delay remains common. The differential diagnosis includes a wide range of benign melanocytic, epithelial, vascular, and infectious lesions.

1.1.3. Treatment and survival

Surgical excision remains the cornerstone of treatment, with function-preserving approaches preferred whenever feasible. Sentinel lymph node biopsy (SLNB) is routinely recommended for staging, with AM showing relatively high rates of nodal involvement. While immune checkpoint inhibitors have improved melanoma outcomes overall, response rates in AM are generally lower, likely reflecting its low tumor mutational burden and distinct immune microenvironment. Targeted therapies are limited, with KIT alterations representing the most relevant actionable targets in selected patients. Novel combination and immunotherapeutic strategies are under investigation.

ALM is consistently associated with poorer survival compared with other cutaneous melanoma subtypes. This disadvantage is largely attributed to greater Breslow thickness and more advanced stage at diagnosis, although intrinsic biological differences may also contribute. Across studies, Breslow thickness, ulceration, age, and stage at diagnosis remain the strongest prognostic factors, underscoring the critical importance of early detection.

1.2. Factors influencing early detection of malignant melanoma

Early detection is the most important modifiable determinant of melanoma prognosis. Melanomas diagnosed at an early stage are typically treated with simple surgical excision, whereas advanced disease requires complex multimodal treatment and is associated with

substantially higher mortality. Earyl detection is commonly defined by a Breslow thickness of ≤1 mm.

Melanoma detection is a multistep process involving patients, healthcare providers, and the healthcare system. Patient-related factors include melanoma awareness, attitudes toward skin monitoring, and regular skin self-examination (SSE). Female sex, younger age, higher educational and socioeconomic status further favour early detection. Positive attitudes toward early diagnosis and familiarity with melanoma warning signs are consistently associated with thinner tumors, whereas delayed help-seeking behaviour contributes to diagnostic delay.

Physician- related factors are also critical. Melanomas detected during physicians-performed skin examinations–particularly by dermatologists–are generally diagnosed at earlier stages. However, time constraints, and lack of routine skin examination during medical visits represent important barriers. Healthcare system factors, including access to dermatologic care, socioeconomic status, and public awareness initiatives, further influence diagnostic timing.

To systematically assess determinants of melanoma detection, the Melbehav questionnaire was developed and used in the United States and later in Greece. These studies demonstrated that regular SSE and dermatologic screening are key determinants of early detection. Central–Eastern European studies, including Hungarian and Romanian cohorts, show improving trends in Breslow thickness over time and highlight the role of education, awareness campaigns, age, and sex in earlier diagnosis. Physician-led screening programs, particularly risk-stratified approaches, improve detection of suspicious lesions, although effectiveness varies by population and country. Targeted screening of high-risk groups appears more beneficial than population-wide screening, which remains controversial and is associated with high costs.

2. AIMS

2.1. Acral lentiginous melanoma: a single-center retrospective review

Acral melanoma is a rare but clinically relevant melanoma subtype; however data from Central–Eastern Europe remain limited. The aims of our work were to address key knowledge gaps in acral melanoma using the long-term experience of a single dermato-oncology center, with particular focus on epidemiology, clinicopathological characteristics, survival outcomes, prognostic factors, and diagnostic delay. In addition, we thought to compare our findings with published international data. Through this center-based analysis, we aimed to provide the first detailed characterization of acral melanoma from Central–Eastern Europe.

The specific aims were as follows:

- To describe the demographic, clinical, and histopathological characteristics of acral melanoma diagnosed at our center over a 40-year period.
- To analyse survival outcomes and identify prognostic factors associated with acral melanoma, including patient- and disease-related characteristics.
- To evaluate temporal trends in epidemiology, diagnostic characteristics, and outcomes across four decades, reflecting changes in awareness and therapeutic approaches.
- To contextualize our results by comparing them with previously published international data, thereby contributing novel epidemiological and outcome data from Central–Eastern Europe.

2.2. Factors influencing the early detection of malignant melanoma

The primary aim of this study was to identify patient-, physician-, and healthcare system–related factors associated with early detection of malignant melanoma in a Hungarian single-center cohort, using a standardized questionnaire-based approach.

The specific aims were as follows:

- To characterize patient and tumor characteristics associated with melanoma thickness.
- To investigate melanoma patients' awareness, knowledge, attitudes, and preventive behaviors—including skin self-examination practices—and their association with melanoma thickness.
- To evaluate medical access, health care use, and physician skin examinations in relation to early melanoma detection.
- To analyse the circumstances of melanoma recognition (patient-, layperson-, or physician-detected) and their relationship to Breslow thickness at diagnosis.
- To compare the findings of this cohort with previously published international studies from the United States and Greece using the same questionnaire.

3. MATERIALS AND METHODS

This work comprised two studies conducted at the Department of Dermatology and Allergology, Albert Szent-Györgyi Health Center, University of Szeged.

3.1. Acral lentiginous melanoma: a single-center retrospective review

We conducted single-center, retrospective cohort study over a 40-year period (1976–2016) including patients diagnosed with acral melanoma. Because anatomical definitions and classification criteria for acral melanoma vary across the literature, and because the acral lentiginous subtype represents the predominant histotype in acral locations, we defined our study population using combined anatomical and histopathological criteria. Eligible cases included melanomas exhibiting acral lentiginous histological subtype and arising on the glabrous skin of the extremities (palms, heels, soles, fingers) or within the nail apparatus. Based on these criteria, the term *acral lentiginous melanoma* was used throughout the study as the most precise and consistent designation.

3.1.1. Patients and data collection

More than 25,000 histopathological reports were reviewed. Inclusion criteria comprised patients with a histologically confirmed diagnosis of invasive acral lentiginous melanoma arising on glabrous skin of the extremities (palms, soles, heels, fingers) or subungual regions. Exclusion criteria included melanoma *in situ*, non-ALM histological subtypes at acral sites, and cases with incomplete or missing key clinicopathological data. Clinical and pathological data were extracted from handwritten medical records for the period of 1976–1996 and from the institutional electronic database (Medsolution) for 1997–2016. Collected variables included patient demographics, primary tumor characteristics (anatomical site, macroscopic appearance, Breslow thickness, Clark level, ulceration), sentinel lymph node (SLN) status, disease stage according to the AJCC 8th edition TNM classification, and treatment modalities. Patient-related diagnostic delay was defined as the time interval between the patient's initial recognition of the lesion and the first consultation with a physician. Temporal trends in incidence, Breslow tumor thickness, and survival were evaluated, and findings were descriptively compared with international data.

3.1.2. Statistical analysis

Overall and disease-specific survival probabilities were estimated using the Kaplan–Meier method, with group comparisons performed using the log-rank test, applying Bonferroni correction for multiple comparisons where appropriate.

Differences in mean Breslow thickness between SLN-positive and SLN-negative patients were evaluated using Student's t-test. Temporal trends in patient age and Breslow thickness were analysed using analysis of variance (ANOVA) and Poisson regression, as appropriate.

The impact of clinicopathological variables on survival was assessed using univariate and multivariate Cox proportional hazards regression models. Covariates included: gender, Clark level (II/III vs. IV/V), ulceration, dermal mitotic rate ≥1/mm², tumor site (hand vs. foot), SLN status, nodal involvement, presence of distant metastases. Age and Breslow thickness were treated as continuous variables. Variables showing a p-value < 0.05 in univariate analyses were entered into the multivariate model, and a p-value < 0.001 was regarded as statistically significant. All analyses were performed using R statistical software (version 3.2.1).

3.2. Factors influencing the early detection of malignant melanoma

Determinants of early melanoma detection were investigated in a prospective, questionnaire-based study conducted over a one-year period in 2015.

3.2.1. Patients and the Melbehav questionnaire

All adult patients diagnosed with malignant melanoma between January and October 2015 were eligible for inclusion. Patients were stratified by Breslow thickness into three groups: melanoma *in situ*, invasive melanoma with Breslow thickness ≤1 mm, and invasive melanoma with Breslow thickness >1 mm. Early detection of a primary melanoma was defined with a Breslow thickness of ≤1 mm and no clinical or radiological evidence of locoregional and/or distant metastases at the time of diagnosis. Patient-, physician-, and healthcare system-related determinants of early detection were assessed using the validated Melbehav questionnaire, developed by Susan M. Swetter *et al.* and previously validated in cohorts from the US and Greece. The instrument comprises 74 items covering 10 thematic domains. The questionnaire was translated into Hungarian and pilot-tested for clarity and feasibility prior to administration. To contextualize our results, key findings were compared with published data from the US and Greek melanoma cohorts. Patients were excluded if key clinicopathological or questionnaire data were incomplete or missing.

3.2.2. Statistical analysis

Associations between potential predictors and early detection were analysed using chi-square tests, Fisher's exact test, and Spearman's rank correlation, as appropriate. All analyses were conducted using R statistical software (version 3.2.1), with p-value <0.05 considered statistically significant. Comparisons with cohorts from the US and Greece were conducted in a qualitative and descriptive manner, relying on reported proportions and associations, and did not include direct statistical testing between populations.

3.3. Ethical considerations

Both studies were conducted in accordance with the Declaration of Helsinki and were approved by the National Council of Health Sciences, Scientific and Research Ethics Committee, as well as the Regional and Institutional Review Board of Human Investigations at the University of Szeged (registration number: 40/2015 (3521), protocol number: MEL-RETRO-001; registration number: 36/2015 (3518) , protocol number: MEL-PREVENT-001).

4. RESULTS

4.1. Acral lentiginous melanoma: a single-center retrospective review

Between 1976 and 2016, 4,593 patients were diagnosed with cutaneous malignant melanoma at our center. Among these, 176 cases (3.83%) were histologically confirmed acral lentiginous melanoma arising on glabrous skin of the extremities or subungual regions.

4.1.1. Patient demographics and primary tumor characteristics

All patients were Caucasian ethnicity. The mean age at diagnosis was 66.2 years, with nearly three-quarters diagnosed after the age of 60. The male-to-female ratio was 1:1.26. ALM occurred predominantly on the lower extremities (88.6%); subungual melanoma accounted for 14.2% of cases. The mean Breslow thickness was 3.86 mm, with 75% of tumors exceeding 2 mm and 37.5% exceeding 4 mm. Clark invasion level IV–V was present in 56.3%, and histological ulceration in 71.6% of cases. Patient-related diagnostic delay was substantial: the mean delay from lesion recognition to physician consultation was 18 months, with over half of patients waiting longer than one year.

4.1.2. Survival and prognostic factors

Five- and ten-year overall survival rates were 60.5% and 41.6%, respectively. Disease-specific survival differed significantly by TNM stage and Breslow thickness ($p < 0.001$). Five-year disease-specific survival decreased from 92.3% in T1 tumors to 28.6% in T4 tumors. Stage I patients showed markedly better outcomes than those with stages II–IV.

SLNB, introduced in 1999, was performed in 32.9% of patients with a high positivity rate (60.3%), and was strongly associated with increased Breslow thickness and poor survival.

Univariate analysis identified age, sex, Breslow thickness, Clark level, ulceration, SLN status, nodal involvement, and distant metastases as significant prognostic factors. In multivariable Cox regression analysis, increasing age (HR 1.058, 95% CI 1.035–1.083), greater Breslow

thickness (HR 1.187, 95% CI 1.099–1.282), and presence of distant metastases (HR 3.002, 95% CI 1.850–4.871) were independent predictors of worse disease-specific survival.

4.1.3. Temporal trends and treatment patterns over four decades

Across four decades no significant change was observed in mean Breslow thickness or patient age at diagnosis. While the absolute number of ALM cases remained stable, their relative proportion declined due to a marked increase in SSM.

All ALM patients underwent wide local excision. Surgical management evolved from elective lymph node dissection to SLNB-based staging. Overall survival improved after 1999, coinciding with changes in surgical practice and staging accuracy. Systemic treatment evolved over time, with dacarbazine and interferon-alpha used in earlier decades, followed by the introduction of targeted and immunotherapeutic agents after 2015. Modern systemic therapies were introduced late in the study period and were used in a limited number of patients.

4.1.4. Comparison with international cohorts

Patient demographics and anatomical distribution were comparable to other European ALM cohorts. However, mean Breslow thickness in our population was among the highest reported.

4.2. Factors influencing the early detection of malignant melanoma

4.2.1. Patient demographics and primary tumor characteristics

A total of 139 questionnaires were analysed. Mean age of patients was 59 years, with equal sex distribution. Thirty-seven percent of melanomas were thicker than 1 mm. Nearly half of patients were older than 60 years, and thicker melanomas were more frequent in this age group. The mean Breslow thickness was 1.65 mm. SSM was the predominant subtype, particularly among thin tumors, whereas nodular melanoma was more frequent in thicker lesions. The trunk and lower extremities were the most common tumor locations. Increasing tumor thickness was associated with older age, ulceration, nodular histology, and trunk or lower-extremity location. No significant associations were observed with sex, educational level, or marital status.

4.2.2. Melanoma patients' preventive behaviours, including skin self-examination

General health awareness was high, as reflected by participation in cancer screening programs and cardiovascular monitoring. In contrast, melanoma-specific preventive behaviors were limited. Regular use of sunscreen or protective clothing was reported by fewer than one-third of patients. Skin self-examination was infrequent or incomplete and was not associated with thinner melanoma at diagnosis. Only 4% of patients used melanoma-specific visual reference

materials during SSE. Partner or family assistance in skin monitoring was common but not linked to earlier detection.

4.2.3. Knowledge and attitudes of melanoma patients toward skin cancer

Although most patients considered themselves health-conscious, few actively sought information on skin cancer. Patients' knowledge and risk perception were limited. Most underestimated their melanoma risk and lacked awareness of melanoma severity prior to diagnosis. Importantly, patients who regarded monitoring suspicious lesions as unimportant were diagnosed with significantly thicker tumors.

4.2.4. Healthcare utilization and provider communication

Despite frequent healthcare utilization–most patients had at least one healthcare encounter in the year preceding diagnosis–physician-performed skin examinations occurred in fewer than one-third of medical visits. Melanoma-specific counselling about melanoma risk, self-monitoring, or atypical nevi was rare.

4.2.5. Circumstances of initial melanoma detection

Patients were the most frequent first detectors of melanoma. Melanomas detected by physicians–particularly dermatologists–were significantly thinner than those detected by patients or laypersons. Delays in seeking medical care were primarily driven by low perceived concern rather than limited access to healthcare, as diagnostic work-up proceeded rapidly following the initial consultation.

5. DISCUSSION

5.1. Acral lentiginous melanoma: a single-center retrospective review

This long-term, single-center study represents the first comprehensive analysis of acral lentiginous melanoma in Central–Eastern Europe. ALM accounted for 3.8% of all melanomas. Mean Breslow thickness approached 4 mm, with three-quarters of tumors exceeding 2 mm. ALM predominantly affected elderly patients, with a mean age of 66 years. Patient demographics and anatomical distribution were comparable to other Caucasian cohorts; however, tumor thickness at diagnosis was among the highest reported in Europe.

Survival outcomes were inferior to those reported in most European and North American ALM studies. Five- and ten-year overall survival rates were markedly reduced and strongly dependent on stage and tumor thickness. Increasing age, Breslow thickness, and distant

metastases emerged as the strongest independent predictors of poor prognosis, emphasizing the critical importance of early detection. Diagnostic delay was substantial, with more than half of patients postponing medical consultation for over one year, supporting its central as a major driver of advanced-stage presentation and adverse outcomes.

Although melanoma management evolved over the four decades studied, no meaningful reductions in Breslow thickness or age at diagnosis were observed. While overall survival improved modestly over time, treatment heterogeneity and low patient number limits definitive conclusions regarding therapy-specific survival benefits.

Despite a substantial increase in overall melanoma incidence at our center—largely driven by UV-related subtypes—the incidence and clinical profile of ALM remained stable, supporting the concept that ALM pathogenesis is largely independent of ultraviolet exposure.

In conclusion, ALM in our region continues to be diagnosed at an advanced stage with excessive tumor thickness and poor outcomes. Diagnostic delay represents the most important modifiable prognostic factor, highlighting the urgent need for targeted educational interventions aimed at elderly populations and healthcare professionals to improve early recognition of ALM.

5.2. Factors influencing the early detection of malignant melanoma

This study provides the first Central–Eastern European data on early melanoma detection using the standardized Melbehav questionnaire, enabling direct comparison with US and Greek cohorts.

Melanomas thicker than >1 mm were associated with older age, nodular histology, ulceration, and an overall unfavourable prognostic profile. More than one-third of tumors exceeded 1 mm in thickness and were most frequently located on the trunk and lower extremities.

In contrast to US and Greek populations, early melanoma detection in our cohort was not associated with demographic characteristics, educational level, marital status, or self-examination practices. Instead, earlier detection was strongly linked to patients' attitudes toward skin monitoring and the perceived importance of early diagnosis.

Although skin self-examination was commonly reported, it was ineffective in the absence of melanoma-specific knowledge. The use of visual reference materials was rare, and most patients underestimated both their personal melanoma risk and the seriousness of the disease–misconceptions that often persisting even after diagnosis. These findings indicate that self-examination alone is insufficient without adequate education on melanoma warning signs.

Despite frequent healthcare utilization, preventive counselling and physician-initiated skin examinations were uncommon, representing missed opportunities for early detection. Routine medical visits rarely included full-body skin examinations or melanoma-related counselling. While patients most often detected their own melanomas, lesions identified by physicians—particularly dermatologists—were diagnosed at significantly thinner stages, underscoring the superior effectiveness of professional skin examination.

Overall, these findings demonstrate that determinants of early melanoma detection are population- and healthcare system–specific. Prevention strategies effective in other countries cannot be directly extrapolated to Central–Eastern Europe without contextual adaptation. Improving patient education, risk perception, and proactive physician involvement is essential to reduce diagnostic delay and improve melanoma outcomes in this region.

5.3. Strengths and limitations of the studies

This thesis integrates two complementary studies that provide novel insights into melanoma detection in a Central–Eastern European setting. The strengths and limitations of each study should be considered when interpreting the results.

The main strength of the retrospective, single-center analysis is that it represents the first comprehensive regional evaluation of ALM, spanning four decades and enabling assessment of clinicopathological characteristics, survival outcomes, prognostic factors, and temporal trends. Clearly defined inclusion criteria ensured a homogeneous cohort, and standardized survival analyses allowed identification of independent prognostic determinants.

Limitations include the retrospective design, potential selection and recall bias, and limited generalizability. Changes in staging systems, diagnostic practices, and treatment modalities over time, as well as the limited availability of molecular data and modern systemic therapies, may have influenced survival analyses. International comparisons were descriptive due to methodological heterogeneity.

A key strength of the second study is the use of the validated Melbehav questionnaire, enabling systematic evaluation of patient-, physician-, and healthcare system–related factors and direct comparison with US and Greek cohorts. Integration of questionnaire and clinicopathological data enhanced the clinical relevance of the findings. Limitations include reliance on self-reported data, possible recall and social desirability bias, a modest sample size, and the descriptive nature of international comparisons. Cultural and healthcare system differences may also have influenced questionnaire responses.

6. CONCLUSIONS

6.1. Acral lentiginous melanoma: a single-center retrospective review

Our study provides novel regional data on epidemiology, clinicopathological features, survival, and diagnostic delay of ALM. The findings underscore the persistent clinical challenges associated with this melanoma subtype, particularly including delayed diagnosis, advanced disease stage at presentation, and its consistently unfavourable prognosis.

Key conclusions:

- This study represents the first comprehensive, long-term, single-center cohort analysis of acral lentiginous melanoma from Central–Eastern Europe, addressing a major gap in regional melanoma epidemiology and outcome data.
- Acral lentiginous melanoma is a rare melanoma subtype that predominantly affects elderly patients and is characterized by unfavourable histopathological features and advanced stage at diagnosis.
- Survival in acral lentiginous melanoma is poor, with age, Breslow thickness and stage at diagnosis representing the main independent prognostic factors.
- Across four decades, no substantial changes were observed in epidemiology, tumor thickness, or patient age at diagnosis.
- Demographic and anatomical characteristics of ALM were largely comparable to other Caucasian cohorts; however, Breslow thickness was among the highest reported.

6.2. Factors influencing the early detection of malignant melanoma

This single-center study identified patient-, physician-, and healthcare system–related determinants of early melanoma detection in a Central–Eastern European population. Early detection was primarily driven by patients' attitudes toward skin monitoring and the perceived importance of early diagnosis, rather than demographic, educational, or social characteristics. Although skin self-examination was commonly reported, it was ineffective in the absence of melanoma-specific knowledge and guidance.

Key conclusions:

- This study provides the first Central-Eastern European data on early melanoma detection using a previously developed, standardized questionnaire.

- Greater Breslow thickness (>1 mm) was associated with unfavorable clinicopathological profile, including older age at diagnosis, ulceration, and nodular subtypes, while no clear association was observed with gender or eductional level.
- Early melanoma detection depend primarly on patients' attitudes toward skin monitoring and the percieved importance of early diagnosis, while skin self-examination alone– without melanoma-specific knowledge–was insufficient to ensure early detection.
- Despite frequent healthcare utilization, low rates of physician-performed skin examination and melanoma-specific counseling represented substantial missed opportunities for early detection.
- Melanomas detected by healthcare professionals were diagnosed at significantly thinner stages than those identified by patients or laypersons.
- Determinants of early detection differed from those reported in the US and Greek cohorts, underscoring the need for region-specific, healthcare system-adapted early detection strategies.

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